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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,111	11/22/2005	George Yousef	MTS13AUSA	8522

270 7590 03/12/2007

HOWSON AND HOWSON
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EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,111	YOUSEF ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 30-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 30-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *February 28, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *petition decision (PTO-90C)*.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/526111	11/22/2005	Yousef et. al.	

EXAMINER
Anne M. Gussow

ART UNIT	PAPER
1643	20070305

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

In re application of Yousef et al.
Serial No. : 10/526111
Filed: November 22, 2005

DECISION ON PETITION
This is in response to applicants' petition, filed on 9/23/02 under 37 CFR 1.84(a), to accept color photographs.
Applicant has fulfilled all requirements of 37 CFR 1.84(a).
Applicants' petition is GRANTED.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Larry R. Helms
Supervisory Patent Examiner
Art Unit 1643

DETAILED ACTION

1. Applicant's election of Group 1, claims 5 and 30-41, in the reply filed on December 26, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. New claims 30-41 have been added.

Claims 3-4, 6-7, and 10-29 have been cancelled.

Claims 5 and 30-41 are under examination.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on February 28, 2005 and December 26, 2006 have been fully considered and initialed copies of the IDSs are included with this Office Action.

Drawings

4. Color photographs have been submitted with this application in three copies accompanied by the appropriate fee set forth in 37 CFR 1.17(h), a petition to enter color drawings, and an amendment to the first paragraph of the brief description of the drawings section of the specification.

The petition has been granted and a signed copy of the petition decision is included with the mailing of this office action.

Specification

5. The disclosure is objected to because of the following informalities:

a.) The specification contains typographical errors, for example, on page 4 line 6 "omparing" should read "comparing" and on page 8 line 13 "show" should read "shows".

b.) The description of Figure 4 on page 8 does not describe parts A and B of Figure 4.

Appropriate correction is required for all errors throughout.

6. The use of the trademarks Sepharose® and HiTrap™ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The trademark symbols are not included for Sepharose® and HiTrap™. Appropriate correction is required for all trademarks throughout.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5 and 30-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a.) Claim 5 is indefinite for reciting "a predetermined standard" because it is not clear what standard is being used to compare the level of kallikrein 13. Is it being compared to BSA, total protein, other proteins, or a set amount of kallikrein 13 in a cancer patient or in normal cells?

b.) Claim 31 is indefinite for reciting "antibodies specifically reactive" because it is not clear what is meant by reactive. Typically antibodies bind to antigens. Catalytic antibodies result in chemical reactions. Do the antibodies cause a chemical reaction?

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 5 and 30-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting increased kallikrein 13 protein in ovarian cancer + BREAST CANCER, does not reasonably provide enablement for a method for diagnosing all endocrine cancers by detecting kallikrein 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a method for detecting or screening a subject for endocrine cancer comprising detecting the amount of kallikrein 13 in a biological sample from a subject and comparing said amount of kallikrein 13 detected to a predetermined standard wherein detection of a level of kallikrein 13 in said sample that is significantly different than that of a standard is diagnostic of endocrine cancer, wherein detection comprises using an antibody specific for kallikrein 13 and further comprises detecting a second biomarker.

The specification discloses a method for detecting an increase in kallikrein 13 protein in ovarian cancer using an antibody specific for kallikrein 13 (page 38 lines 4-10 and page 41 lines 33-38). The specification discloses an increase in progression-free survival and overall survival in kallikrein 13 positive patients (page 42 lines 9-18 and figure 8). Applicants have not provided any guidance to assist one skilled in the art in the diagnosis of ovarian cancer or in detection of kallikrein 13 in other endocrine cancers. Further, the as-filed specification fails to address the following issues:

1.) what second biomarkers are indicative of ovarian cancer

2.) what protein level of a second biomarker would be diagnostic for ovarian cancer
3.) what levels of kallikrein 13 are detected in other endocrine cancers such as, pituitary, thyroid, breast, prostate, or pancreatic cancers

It is well known in the art that the majority of cases of ovarian cancer are diagnosed as advanced stage disease and that the response to first-line treatment is largely unpredictable (Canevari, et al. 2006, Critical Reviews in Oncology/Hematology, Vol. 60, pages 19-37). Yousef, et al. (Journal of Biological Chemistry, 2000. Vol. 275 No. 16, pages 11891-11898, as cited on the IDS) teach KLK-L4 (kallikrein 13) expression is reduced at the mRNA level in 16 out of 19 breast cancer tumors (page 11895 2nd column).

In normal tissues kallikrein 13 is expressed in a variety of tissues, including intestine, esophagus, gallbladder, glandular epithelia in the genitourinary tract of males and females, kidney, prostate, ovary, pituitary, peripheral nerves, and neurons and glial cells of the central nervous system (Petraki, et al. Journal of Histochemistry and Cytochemistry, 2003. Vol. 51 No. 4, pages 493-501, as cited on the IDS). Since kallikrein 13 is expressed in many human tissues it cannot be considered a tissue specific marker and without experimental determination of specific kallikrein 13 levels in cancerous cells compared to normal cells cannot on its own be diagnostic.

Regarding second biomarkers diagnostic for ovarian cancer, Bast, et al. (International Journal of Gynecological Cancer, 2005. Vol. 15 Suppl. 3, pages 274-281) teach CA125 levels may be elevated in patients with benign gynecological disease or

non-gynecological disease, however, when monitored over time progressively rising CA125 values are associated with ovarian cancer, whereas stable CA125 values, even when elevated, are associated with benign conditions. Canevari, et al. (supra) teach a number of markers for ovarian cancer including CA125, p53, BRCA, M-CAM, and others (see table 1). Each of these markers have different benefits and drawbacks in screening, for example, the relationship between BRCA alteration and epithelial ovarian cancer survival has been studied extensively with no unequivocal association with better prognosis (page 24 2nd column). Canevari, et al. teach the necessity of validation to confirm the accuracy, precision and effectiveness of new biomarkers (page 30 column 2).

There is insufficient evidence that would lead the skilled artisan to predict the amount of kallikrein 13 necessary to diagnose ovarian cancer or just any endocrine cancer. The specification does not teach how to diagnose cancer based on levels of multiple biomarkers or what levels of kallikrein 13 are expressed in normal endocrine cells other than ovarian cells.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing endocrine cancers, commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 5 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Chang, et al. (British Journal of Cancer, 2002. Vol. 86, pages 1457-1464).

This rejection is consistent with the enablement of the present invention.

The claims recite a method for detecting, or screening a subject for endocrine cancer comprising detecting the amount of kallikrein 13 in a biological sample from a subject and comparing said amount of kallikrein 13 detected to a predetermined standard wherein detection of a level of kallikrein 13 in said sample that is significantly different than that of a standard is diagnostic of endocrine cancer wherein the level of kallikrein 13 is increased in comparison with the standard.

Chang, et al. teach a method for detecting kallikrein 13 in a biological sample of breast cancer by measuring the amount of kallikrein 13 mRNA as compared to the amount of kallikrein 13 mRNA in normal breast tissue with an increased amount of kallikrein 13 predicting increased survival (page 1461 results 1st column, and figure 2). Since the claims do not define a particular endocrine cancer and the method steps recited in the claims are the same as the method steps of Chang, et al. and due to the indefinite nature of the predetermined standard (see 112 2nd paragraph, above), normal

breast tissue levels are considered a predetermined standard, all the limitations of the claims have been met.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow, Ph.D.

March 7, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER